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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/046,922	01/15/2002	Kari Alitalo	28967/37084A	3363

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 08/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/046,922	Applicant(s) ALITALO ET AL.	
	Examiner Phuong Huynh	Art Unit 1644	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 13 June 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *13 June 2005*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered; or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *NONE*.
   Claim(s) objected to: *NONE*.
   Claim(s) rejected: *1-13 and 21-38*.
   Claim(s) withdrawn from consideration: *39-74*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuing pages.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

S.o.o

1. Claims 12, 21, and 22 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants' arguments filed 6/13/05 have been fully considered but are not found persuasive.

Applicants' position is that the Examiner unnecessarily places restrictions in the claimed peptides that are not in the claims. The X1, X2, X3 amino acids specifically identified by the Examiner (LT1) are simply amino acids at these positions exemplified by the specification, and are not limiting. The specification clearly discloses that the residues may be any amino acids (page 16, lines 3-7, and page 17, lines 1 1-16). The specification clearly sets out what any amino acid, and as such, a worker of ordinary skill in the art would have no difficulty determining the metes and bounds of the claimed peptides.

In contrast to applicant's assertion that a worker of ordinary skill in the art would have no difficulty determining the metes and bounds of the claimed peptides, one of ordinary skill in the art would have problem in determining the metes and bounds of the claimed polypeptide without the amino acid sequence. Even the X1, X2, X3 are amino acids, the term "comprising" is open-ended. It expands the formula to include additional amino acids at upstream and down stream of the formula. The specification does not adequate described those additional amino acids.

2. The enablement rejection of Claims 1-13 and 21-38 stands rejected under 35 U.S.C. 112, first paragraph.

Applicants' arguments filed 6/13/05 have been fully considered but are not found persuasive.

Applicants' position is that the term "comprising" is standard claim language accepted by the Patent and Trademark Office which permits a claim to embrace embodiments with additional features beyond what is recited in the claim. In addition, Applicants have fully enabled a worker of ordinary skill in the art to make and use a peptide of 8-100 amino acids comprising the claimed shorter peptides. For example, the specification at page 35, line 8, to page 38, line 6, teaches methods for making peptides of varying lengths using techniques common in the art such as solid phase synthesis, preparation from a phage library, and recombinant expression systems. The specification indicates that a worker of ordinary skill can prepare a phage display library having peptides of a desired length range, e.g., from 4 to about 80 amino acids (Koivunen et al., JNucl.

Med. 40:883-88, 1999., Heiskanen et a1., Virolov 262:321-32, 1999, abstracts included), and also teaches that the peptide may be a part of a fusion protein or a chimeric protein,, e.g. a GST fusion protein (see page 38). Further, the specification provides guidance as to which peptides of the invention would exhibit binding to VEGFR-3. Methods for assaying binding to VEGFR-3 are set forth in the specification (page 42, line 1, to page 53, line 2), and it is well within the skill of the ordinary worker to generate peptides having amino acid substitutions of the peptide sequence and, without undue experimentation, determine if the substituted peptides bind VEGFR-3.

In response, it is the additional feature that is not enabled in the specification as filed. If the polypeptide is a full-length polypeptide, then the use of the term "comprising" is appropriate. However, if the peptide is a fragment, then the term "consisting of" is appropriate. As discussed in the Final rejection, a person skill in the art can only make a polypeptide if the sequence of the polypeptide is known. Without the amino acid sequence, it would require undue experimentation of one skilled in the art to make and use the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In response to applicant's argument that peptide may be a part of a fusion protein or a chimeric protein, e.g. a GST fusion protein, none of the claims recite a fusion protein such as GST fusion protein as argued.

In response to applicant's argument that it is well within the skill of the ordinary worker to generate peptides having amino acid substitutions of the peptide sequence and, without undue experimentation, determine if the substituted peptides bind VEGFR-3, simply binding does not equal a particular biological function. These assays merely extend an invitation to one of ordinary skill in the art come up with the structure of the claimed polypeptide without the amino acid sequence and find therapeutic use for these polypeptides. The rejection stands for reasons of record.

In response to applicant's assertion that claim 13 is allowable, the term "comprises" is open-ended. It expands the peptide of SEQ IDNO: 35 to include additional amino acids at either or both ends of the claimed peptide. There is insufficient guidance as to which amino acids to be added at either or both ends. The rejection stands for reasons of record.

3. Claims 21-22 stand rejected under 35 U.S.C. 102(b) as being anticipated by Hirohashi *et al* (Mol Pharmacol 53(6): 1068-75, June 1998 Jun; PTO 892).

Applicants' arguments filed 6/13/05 have been fully considered but are not found persuasive.

Applicants' position is that Hirohashi's 1502 amino acid protein has never been shown or suggested to bind VEGFR-3 as required by the claims. Although the term "comprising" may be open-ended, the claims specify a peptide whose amino acid sequence is no larger than about 100 amino acids, and Hirohashi's polypeptide is much larger. The claim term comprising permits the inclusion of other elements, such as a label, or toxin, or glycosylation or pegsylation or other modification, but the claim limitation the amino acid sequence consisting of 7-100 amino acids" does not permit the claim to read on a 1502 amino acid protein in the prior art.

In response, Claim 21 recite an isolated peptide *comprising* an amino acid sequence consisting of 7-100 amino acids *comprising* the amino acid sequence GYWX1X2X3W (SEQ ID NO: 67), wherein X1, X2 and X3 comprise amino acids, wherein the peptide binds VEGFR-3. The claimed polypeptide does not limited to 7-100 amino acids as argued. The claim does not recite the polypeptide is conjugated to a label, a toxin or is glycosylated or pegsylated. Given the reference polypeptide appears to have the same structure as the claimed polypeptide, and since the Patent Office does not have the facilities for examining and comparing the binding specificity of the claimed peptide to those of the prior art, the burden is on applicant to show that the prior art peptide is different from the claimed peptide. See In re Best, 562 F.2d 1252, 195 USPQ 430(CCPA 1977).

All rejections remain.

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